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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/220,920	12/24/1998	JEFFREY D. MILBRANDT	6029-7996	5436

7590 09/26/2002

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/220,920	MILBRANDT ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,15-27,39 and 40* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☒ Claim(s) *23,24 and 27* is/are allowed.

6)☒ Claim(s) *12,15-22,25,26,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 11-12, 15-27, 39-40 are pending. Claims 12, 17, 23, 25 and 27 were amended in Paper No. 23, 7/1/2002. Claim 11 stands withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 12, 15-27, 39-40 are under consideration.

Response to Amendment

The rejection of claim 27 under 35 USC § 112 first paragraph for scope of enablement has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claim 27 under 35 USC § 112 first paragraph as lacking written description has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 12 and 25 under 35 USC § 112 second paragraph as being indefinite because it is unclear which polypeptide the 8 contiguous amino acids referred to has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claim 23 under 35 USC § 112 second paragraph has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claim 12 under 35 USC § 112 second paragraph for the recitation of "active domain", has been withdrawn based on Applicant's argument that the term is defined in the specification at page 31, lines 25-30.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 25 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 26, or a nucleic acid encoding an amino acid sequence which is at least 88% identical to SEQ ID NO: 26 which promotes survival of neurons, does not reasonably provide enablement for a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 12, 25 and 39 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of Artemin. The artemin amino acid sequence of SEQ ID NO: 26 is 220 amino acids long, while the claimed polynucleotide need encode only 8 amino acids of artemin. This is only 3.6% of the amino acid sequence, and there is insufficient guidance as to how any particular 8 amino acid stretch would be expected to function to promote the survival of neurons. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of Artemin. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's

function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass variant polyppeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims are drawn to a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin.

(2) the nature of the invention - The instant invention is a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin.

(3) the state of the prior art - The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

(5) the level of predictability in the art - The Voet reference demonstrates the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught a nucleic acid sequence encoding SEQ ID NO: 26.

(7) the existence of working examples - Working examples are not provided for a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 12, 25 and 39 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 12, 25 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions,

deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 2. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid encoding the polypeptide of SEQ ID NO: 26 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 25, 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12, 25, and 39 are vague and indefinite because it is unclear how a polynucleotide could encode a fragment of artemin which is 8 contiguous amino acids long, while also encoding an amino acid which is 88% identical to SEQ ID NO: 26.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 12, 15 and 25 recites the broad recitation "at least 8 contiguous amino acids", and the claim also recites 88% identical to SEQ ID NO: 26

which is the narrower statement of the range/limitation. Claims 16-22, 26, 39, 40 are rejected due to their dependence on claims 12, 15 and 25, as set forth in Paper No. 22, 4/8/2002.

Claims 12, 15, 25 are vague and indefinite in the recitation of the term "biologically equivalent". The term "biologically equivalent " is not defined by the claim, but give no definition of what this equivalence is. Various biological activities can be attributed to a peptide. For example, "biologically equivalent" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Biologically equivalent' could also be referring to the ability of the fragment to stimulate antibody production. Claims 16-22, 26, 39, 40 are rejected due to their dependence on claims 12, 15 and 25.

Applicant argues that the term "biologically active" is defined in the Specification on page 21, lines 2-5. However, this is a definition of the term "biologically active" not a definition of the term "biologically equivalent". It is not clear that the equivalence needs to be a function or activity, and the criteria which are to be used to determine the equivalence are not set forth in the specification.

Claims 12, 15 and 25 are indefinite in the recitation of the term "naturally occurring". It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from tissue which contains polynucleotides encoding the polypeptide, or if the claim encompasses all polynucleotide sequences that encode the polypeptide. Therefore, the metes and bounds of the claim are unclear. Claims 16-22, 26, 39, 40 are rejected due to their dependence on claims 12, 15 and 25.

Applicant argues that the term naturally occurring is definite because it is used in the art to mean a substance as it is found or occurs in nature. However, it is still not clear whether this claim only encompasses polynucleotides which are isolated from cells extracted from animals, presumably naturally occurring or whether the claim also encompasses polynucleotides isolated from, e.g. cell lines, which are not naturally occurring, but which are derived from animals. It is also not clear whether the claims encompass polynucleotides which are transfected into host cells, and produce a polypeptide, or would the polypeptide produced in this manner no longer be considered "naturally occurring" and thus the encoding polynucleotide would not be encompassed by the claim?

Conclusion

Claims 23-24, 27 are allowable.

Claims 12, 15-22, 25-26, 39-40 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
September 26, 2002